REMARKS

Applicant submits herewith the Declaration of Christos Zouboulis, MD, under 37 C.F.R. §1.132 in support of this Amendment.

Claims 1-6, 8-10; 23-25; 27-31; 33-36; 38-68 are pending and under consideration in the present application. Claim 47, dependent on previously canceled claim7, has been canceled in view of the previous amendment.

In the Office Action of December 1, 2004, the Office allowed claim 10; but rejected claims 1-6, 8, 9, 23-25; 27-31; 33-36, 38, 40, 42, 45, 47 and 63-68 under 35 U.S.C. § 103(a) as allegedly obvious over Zouboulis et al. (Dermatology 196) or Rosenfield (6,004,751) in view of Bryan (Crit. Rev. Onc. 5(4)). This rejection is respectfully traversed for the reasons set forth below and in the Applicant's accompanying declaration under 37 C.F.R. §1.132, which documents how the Applicant overcame the difficulties in immortalizing human sebocytes (*see* March 21, 2006 Office Action at page 3 "It is suggested that a further 132 declaration be provided to detail in length how applicant overcame the problems they have discussed.").

As Applicant has previously noted, Rosenfield is directed to the cultivation of cells of the *preputial gland* derived from a transgenic mouse homozygous for a temperature sensitive strain of SV40T (cf. Example IV), while Zouboulis et al. (Dermatology 196) is directed to the use of *non-immortalized* human sebocytes for the research on seborrhoea and acne. Bryan is generally directed to the immortalization of different human cell types using SV40T. Rosenfield or Zouboulis in view of Bryan does not teach or suggest the present invention. As set forth in Applicant's accompanying declaration under 37 C.F.R. §1.132, the present invention overcomes many of the barriers of the prior art, as exemplified by the unexpected results, long-felt need, the continued failure of others, and the commercial success of the invention.

As set forth in detail in Applicant's accompanying 132 declaration, it was unexpected that the Applicant could successfully obtain immortalized sebocytes suitable for the intended use as described in the present invention. The objective problem underlying the present invention is to provide a human immortalized sebocyte culture having substantially the same properties as a primary sebocyte culture suitable for further investigations in the field of sebocyte-related human skin diseases. This problem is surprisingly solved by the inventive sebocytes.

Prior to the Applicant's invention of the immortalized sebocyte and the immortalized sebocyte cell line disclosed in the present application, numerous scientific groups and companies had tried but failed to obtain immortalized sebocytes. What the declaration establishes is that applying known techniques will not yield immortalized sebocyte cells or immortalized sebocyte cell lines. Rather, as the declaration explains, special steps are necessary, including transfection by lipofection and selection of sebocytes from mature individuals.

The Applicant began work on the isolation and *in vitro* cultivation of human sebocytes in the 1980's, and this work was published in the Journal of Investigative Dermatology, vol. 93, pages 315-321 (1989). Utilizing the techniques set forth in M. Blumemberg et al. in the Journal of Investigational Dermatology, vol. 97, pages 969-973 (1991) on various techniques for immortalizing human epidermal keratinocytes, the Applicant initiated efforts to establish immortalized human sebocytes. Nevertheless, all of the Applicant's initial efforts to immortalize human sebocytes using the techniques set forth in Blumenberg et al. were unsuccessful. Although the Applicant was subsequently successful in immortalizing some cells only by using the lipofection technique; the cells failed to display any of the key characteristics of sebocytes, such as the synthesis of lipids or response to retinoids. The Applicant then embarked on an intensive screening process, attempting immortalize skin cells drawn from many body parts and

many different types of individuals. Because the Applicant had a particular interest in older individuals and particularly facial skin cells from such individuals as a result of Applicant's own data, which became available in early 1995, that such cells did not proliferate or did not proliferate well, the Applicant then focused his efforts on mature cells, for example from individuals 50 years or older.

The Applicant was finally successful in obtaining immortalized sebocytes from the facial cells of an 87 year old woman. Initially, the cells did not grow at all. The Applicant nevertheless kept the cells under observation for approximately three months. Surprisingly, these cells proved to be immortalized sebocytes on analysis; they produced lipids and the SV 40 T cell antigen characteristic of the immortalizing agent. This result was published in the Journal of Investigational Dermatology, vol. 113, pages 1011-1020 (1999).

The Applicant's unexpected success in achieving immortalized sebocytes and a sebocyte line have generated considerable interest in the pharmaceutical and cosmetic industry, as well as the scientific community.

Although there is a great international need for immortalized sebocytes, no one has independently developed immortal sebocytes using other techniques. The one successful effort to develop an additional immortalized sebocyte cell line of which Applicant is aware utilizes the procedures outlined in Applicant's 1999 article (which are likewise set forth in the present application). *See* Thiboutot et al., Journal of Investigational Dermatology, vol. 120, pages 905-914 (2003).

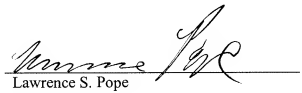
In addition, the Applicant has successfully licensed the immortalized sebocytes of the present invention to 14 pharmaceutical and cosmetics companies, eight of which have annual

sales in excess of $2 billion annually; nine of which have annual sales in excess of $500 million and eleven of which have annual sales in excess of $100 million.

Furthermore, the Applicant has, upon request, provided samples of the immortalized cells of the present invention to sixty-eight research laboratories worldwide. From this, twenty-nine original manuscripts reporting on research utilizing the immortalized cells of the present invention have been published, and five more have been accepted for publication.

In view of the above, Applicant submits that the rejection of claims 1-6, 8, 9, 23-25; 27-31; 33-36, 38, 40, 42, 45, 47 and 63-68 under 35 U.S.C. § 103(a) as allegedly obvious over Zouboulis et al. (Dermatology 196) or Rosenfield (6,004,751) in view of Bryan (Crit. Rev. Onc. 5(4)) is improper and should be withdrawn.

Respectfully submitted,



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